What is the Question?

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Outline

- Types of Designs
- Types of questions
  - Primary
  - Secondary
  - Ancillary
- Types of Outcomes
- Types of Population

Your Precious Design Time

- 30% of your trial design time should be spent on:
  - Primary question
  - Design statement
  - Lay summary
- 30% further should be spent on:
  - Power analysis
  - Statistical approach
  - Budget

Anatomy of a Primary Question

Given the current state of the literature / science:

What is the next question that needs to be answered?

Overview of FDA Phases

Pre-clinical research:

- Reasonable evidence that the drug is likely to work

Phase I:

- Evaluation of the metabolic and pharmacologic action of a drug, side effects, dosage and toxicity
- Can be used to determine minimally effective dose and maximally tolerated dose
- Typically, participants are healthy volunteers
- Usually conducted with small numbers

FDA Trial Phases

Phase II:

- *Controlled clinical study* conducted to obtain preliminary data regarding the efficacy of a drug in patients with a disease/condition
- Also used to evaluate short-term side effects and risks
- Can be used to determine minimally effective dose and maximally tolerated dose
- Typically involves smaller numbers than in later trials, but more than in Phase I
- May be blinded or unblinded

FDA Trial Phases

Phase III:

- Expanded testing of the drug
- *Randomized, double-blinded trial*, testing the trial drug against either placebo or against the current standard of treatment
- Conducted only after phase II trials have shown evidence of efficacy

FDA Trial Phases

Phase IV:

- Examines long-term outcomes of the drug
- Determines whether drug may be suitable for populations outside those for which it has received FDA approval
- Considers effectiveness and cost of the drug relative to other drugs available for the same condition

Behavioral Trial Phase Equivalents

Preclinical:

- Identify relevant theories and empirical evidence that provide reasonable evidence that the treatment will be efficacious

Behavioral Trial Phase Equivalents

Phase I:

- Evaluation of the proposed mechanism of action of a treatment, side effects (e.g., patient acceptance), dosage
- Can be used to determine minimally effective dose and maximally tolerated dose
- Typically with healthy volunteers
- Usually with small numbers

Behavioral Trial Phase Equivalents

Phase II:

- *Controlled clinical study* conducted to obtain preliminary data regarding the efficacy of a treatment in patients with a disease/condition
- Also used to evaluate the short-term side effects and risks
- Can be used to determine minimally effective dose and maximally tolerated dose
- Smaller numbers than in later trials, but more than in Phase I
- May be blinded or unblinded

Behavioral Trial Phase Equivalents

Phase III:

- Expanded testing of the intervention
- *Randomized, assessor-blinded trial*, with the intervention being tested either against placebo or against the current standard of treatment
- Conducted only after phase II trials have shown preliminary efficacy evidence

Behavioral Trial Phase Equivalents

Phase IV:

- Examines long-term outcomes of the intervention
- Determines whether intervention may be suitable for populations outside those upon which Phase III data was collected
- Considers effectiveness and cost of the intervention relative to other interventions available for the same condition

Type of Trial Questions

- Primary
- Secondary
- Ancillary

Primary Question

Will Exposure to Dosage A of Intervention B

Compared to Control C

Alter Outcome D in Patient Population E?

Primary Question and Trial Phase

The decision of what phase of trial to initiate is determined by the state of knowledge regarding key variables

- Do you have data to support proposed dosage (duration, intensity, timing, of behavioral intervention)?
- What controls have been used? What is next level of control needed?

Primary Question

You can only have one!

Secondary Question

- Different outcome
- Component of the Composite Primary outcome
- Subgroup analysis

Ancillary Questions

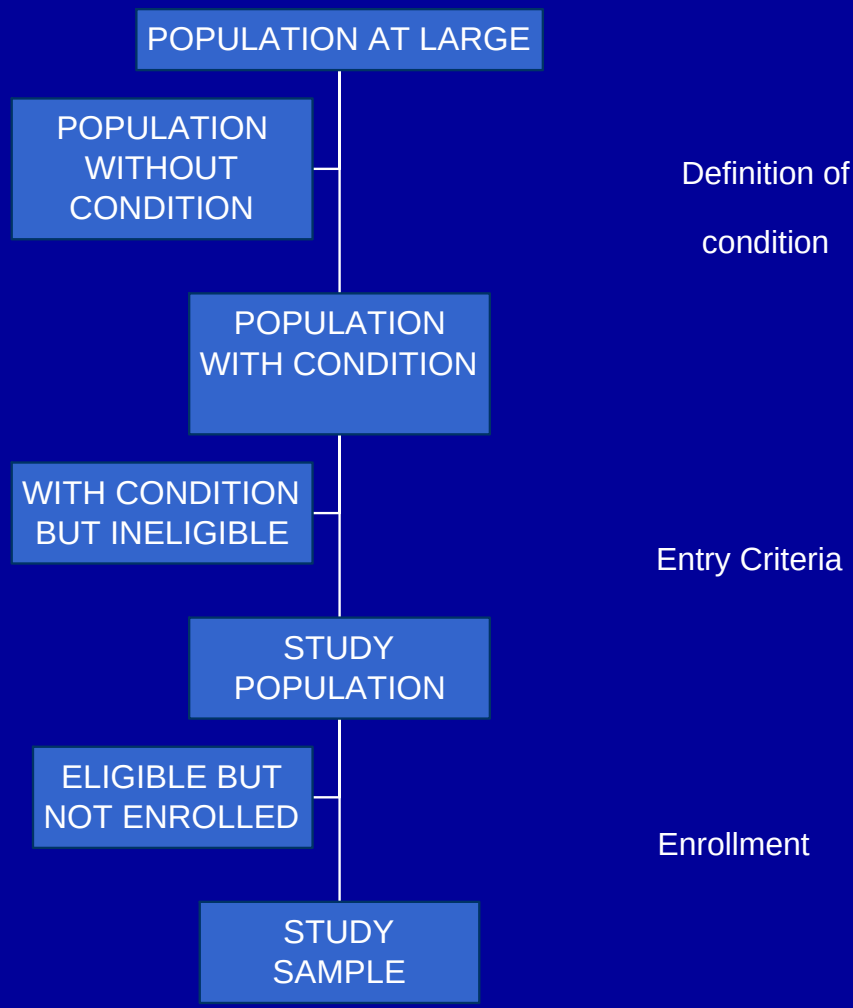
- Natural history (in control group)
- Additional substudy
- Registry of refusers
- Additional comparison group (e.g., low risk/non-disease)

Types of Outcomes

- Gold standard
- Composite
- Surrogate
- Mechanism
- Adverse events
- Patient / provider / system acceptance
- Cost

Types of Outcomes

- Objective assessment
- Masked assessment
- Unbiased ascertainment


POPULATION AT LARGE
POPULATION WITHOUT CONDITION
POPULATION WITH CONDITION
WITH CONDITION BUT INELIGIBLE
STUDY POPULATION
ELIGIBLE BUT NOT ENROLLED
STUDY SAMPLE
Definition of condition
Entry Criteria
Enrollment